SYNTHESIS AND QUALITY CONTROL OF ALIPHATIC AND AROMATIC ^{18}F-LABELLED COMPOUNDS FOR PROBING METABOLISM IN-VIVO

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Biomolecules tagged with fluorine-18, a positron emitter with a half-life of 110 min, are gaining importance in diagnostic nuclear medicine for measuring regional functions in-vivo by means of positron emission tomography. Procedures for introducing ^{18}F into organic compounds, however, are limited due to the short half-life. In addition, the toxicity of many fluorine compounds requires practically carrier-free products. Hence, fast syntheses have to be carried out using fluorinating agents in the micro- or nanogram scale. On the other hand, the tracer provides unique possibilities for studying metabolic functions of toxic or centrally active fluorine compounds in-vivo. We have synthesized several aliphatic and aromatic fluorine-18 labelled compounds by nucleophilic ^{18}F-for-halogen exchange: For the study of regional metabolism in heart and liver of mice 16-^{18}F-hexadecanoic acid, 17-^{18}F-heptadecanoic acid, 2-^{18}F-, and (9,10)-^{18}F-stearic acid were prepared in a mixture of molten acetamide and the corresponding bromofatty acid ester followed by hydrolysis and purification by high pressure liquid chromatography. Variation of temperature, reaction time, and KF-carrier finally led to an optimum radiochemical yield of about 30% [1].

The biochemical effects of the fluorine label, as expected on the basis of ß-oxidation, is clearly reflected in the pharmacokinetics and the chemical fate of the fluorine label observed in mice: The odd-numbered compound, 17-^{18}F-heptadecanoic acid, is catabolized to ß-^{18}F-propionic acid while the even-numbered 16-^{18}F-hexadecanoic acid ends up

with ^{18}F-fluoroacetic acid entering the citric cycle. Further degradation, i.e. dehalogenation, only occurs in the case of 17-^{18}F-heptadecanoic acid yielding free ^{18}F-fluoride which can be detected in high yield among its metabolites [2].

With respect to diagnostic methods for the localisation of thrombi, the protein urokinase labelled with ^{18}F-fluoroacetic acid could be a useful compound, since it is expected that it will be concentrated in the thrombus thus giving the possibility of localisation by positron-emission tomography. ^{18}F-fluoroacetic acid has therefore been prepared carrier-free in order to prevent the occupation of active sites in urokinase.

For the study of regional metabolism in brain, 2-^{18}F-nicotinic acid diethylamide is potentially useful. The nonhalogenated compound is known to be a centrally acting pharmaceutical. Preparation of the ^{18}F-labelled compound was carried out by a similar procedure as in the case of the fatty acids starting from the corresponding chloro-compound. By this method optimum radiochemical yields up to 46% could be obtained. Preliminary results in experiments with mice show a fast accumulation of ^{18}F-activity in the brain within the first seconds after injection, followed by a slower decrease [3].

1 F.J. Knust, M. Schüller, and G. Stöcklin - J Lab Comp.